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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,531	01/25/2002	Jeffrey A. Lyon	003/241/SAP	2343

7590 05/04/2004

U. S. Army Medical Research and Materiel Command
ATTN: MCMR-JA (Ms. Elizabeth Arwine- Patent Atty)
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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,531	LYON ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-2, 15-47 and 49 -52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-14 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The response to the First Action On Merits filed on 2/4/04 has been entered into the record.

Status of Claims

2. Claims 1-52 are pending in the application.

Claims 3-14 and 48 are under examination.

Claims 1-2, 15-47 and 49 -52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected group.

Information Disclosure Statement

3. The information disclosure statement filed on 2/4/04 is acknowledged and a signed coy of the same is attached to this office action.

Claim Rejection and Objection Withdrawn

4. In view of amendment to the claim 5, the rejection under 35 U.S.C.112, second paragraph is withdrawn.

In view of amendment to the claim 3, the objection is withdrawn for minor informalities.

Specification Informalities Maintained

5. Applicant states that the amendment to the specification will be made after receiving the ATCC depository information. Therefore, the objection of the disclosure for lack of complete information in the specification on page 6, ATCC address and plasmid pETATpfMSP-1_{42}(3D7) accession number is maintained.

Claim Rejections - 35 USC 112, first paragraph Maintained

6. The rejection of claims 3-14 and 48 under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure without complete evidence that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of biological material, ATCC pETATpfMSP-1_{42} (3D7) is maintained for the same reason as stated above in paragraph # 5.

Claim Rejections - 35 USC 102 Maintained

7. The rejection of claim 3 under 35 U.S.C. 102(b) as being anticipated by Kumar et al 1995, Molecular Medicine 1, 325-332 is maintained for the same reason as set forth in the previous office action.

Kumar et al disclose a recombinant vector pGEX3 comprising a DNA sequence encoding MSP-1_{42} (see page 326, left column, third paragraph under Materials and Methods). Thus the prior art anticipates the claimed invention.

8. The rejection of claim 3 under 35 U.S.C. 102(b) as being anticipated by Chang et al 1996, Infection and Immunity 64: 253-261 is maintained for the same reason as set forth in the previous office action.

Chang et al disclose a recombinant vector baculovirus comprising a DNA sequence (BV 42) encoding MSP-1_{42} (see page 254, left column, first paragraph under Materials and Methods) Thus, the prior art anticipates the claimed invention.

Applicants' arguments filed on 2/4/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the claim 3 is amended to recite the characteristic that "expression of said vector under suitable condition results in a protein that retains its native folding", and is believed to be free of the rejection.

It is the position of the examiner that the applicant has not provided any evidence to show that the claimed recombinant vector is different from the disclosed recombinant vector, wherein expression of a protein induced by IPTG resulted in a protein that retains native folding. Therefore, in the absence of evidence to the contrary the recombinant vector as disclosed by either Kumar et al or Chang et al read on claim 3. Hence this rejection is maintained.

9. The rejection of claims 9-10 under 35 U.S.C. 102(b) as being anticipated by Kumar et al 1995, Molecular Medicine 1, 325-332 is maintained as set forth in the previous office action.

Kumar et al disclose a method of producing and purifying recombinant MSP-1_{42} (see page 326, left column, third paragraph through right column under Materials and Methods) from *P.falciparum*. The recombinant plasmid pGEX3 was electroporated in to E.coli. Bacterial cells were grown in the presence of IPTG at 25°C to induce the high expression of recombinant protein, said cells were lysed by sonication. Recombinant protein bound to a reduced glutathione –agarose column and eluted with 10mM reduced glutathione (see page 326left column through right column under protein purification of rGST-MSP1-$_{42}$. The recombinant MSP-1_{42} that recovered was used as a vaccine in Aotus Monkeys (see page 327, right column last paragraph). Thus the prior art anticipated the claimed invention.

Applicants' arguments filed on 2/4/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that Kumar et al does not disclose a method wherein host cells are grown such that a vector expressing *P. falciparum* MSP-1_{42} expresses a soluble protein, and the host cells are lysed so that protein is recovered that retains its native folding. Further applicant states that the prior art does not disclose the expression of the vector is induced by IPTG at a temperature range of 24°C-27°C as recited in claim 10.

It is the position of the examiner that the applicant has not provided any evidence to show that the claimed method is different from the disclosed method wherein expression of a protein in a vector induced by IPTG resulted in a protein that retains native folding. Therefore, this rejection is maintained.

Claim Rejections - 35 USC § 103 Maintained

10. The rejection of claims 9-14 and 48 under 35 U.S.C. 103(a) as being unpatentable over Kumar et al 1995, Molecular Medicine 1, 325-332 in view of Short Protocols in Molecular Biology Ed: Ausubel Publisher: John Wiley, especially see pages 10-59, 16-31, 16-32, 16-33 and16-34 is maintained for the same reason as set forth in the previous office action.

Kumar et al teaches a method of producing and purifying recombinant *P.falciparum* MSP-1_{42} (see page 326, left column, third paragraph through right column under Materials and Methods) from vector pGEX3. The recombinant plasmid was electroporated into E.coli. Bacterial cells were grown in the presence of IPTG to induce to produce recombinant protein, said cells were lysed (sonication) and recombinant protein was recovered. However, the prior art does not teach said using vector pETATpf MSP1-$_{42,}$ host cells lysed in the presence of imidazole and E.coli endotoxin removed by application to a Ni-NTA column in said method. However, Ausubel teaches protein expression in various vectors including thioredoxin fusion proteins, growing the expression vectors containing DNA encoding proteins that are induced by IPTG at various temperatures in the presence of fungicides, antibiotics and purifying proteins from E.coli containing pET vectors using Ni- NTA column (especially see pages 10-59, 16-31, 16-32, 16-33 and16-34) to remove endotoxin etc as it is routine in the art. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a method for producing recombinant *plasmodium falciparum* protein as taught by Kumar and use the routine technology in the art including various temperatures to induce high yield of recombinant product, growing cells in large amounts in the presence of fungicides such as imidazole or other antibiotics, lysing cells and purifying the protein using NTA column as taught by Ausubel (see page 10-59) with a reasonable expectation of success because it would help in preparing pure recombinant MSP1-$_{42}$ protein from any vector including pETATpf MSP1-$_{42}$ An artisan of ordinary skills would have been motivated in applying the methods of Kumar et al to the Ausuble methods to purify and obtain large quantities of soluble protein because the prior art suggests that protein could be used in a vaccine preparation (see Kumar's abstract) or in diagnostic assays. The claimed invention is prima facie obvious over Kumar et al in view of Ausuble absent any convincing evidence to the contrary.

Applicant states that the combination of Kumar and Ausuble are no more than an "invitation to experiment", which would have required applicants to pick and choose among the myriad of protocols described in Ausubel.

The examiner disagrees with the applicant because the examiner has established a clear prima facie obvious over Kumar et al (as discussed above in paragraphs # 8 and 9) in view of Ausuble because Kumar et al teach a method for producing a recombinant *plasmodium falciparum* protein MSP1-$_{42}$ using vector pGEX3 and does not disclose pETAT expression

vector. However, it is routine in the art to obtain high yield of recombinant product by growing cells in large amounts in the presence of fungicides such as imidazole or other antibiotics, lysing cells and purifying the protein using NTA column using pETAT expression vector system. Ausubel (see page 10-59) disclosed myriad of protocols of various aspects of molecular biology. However, pETAT is one of the expression vector systems that is routinely used to obtain large amounts of protein and is taught by Ausubel. Selecting an expression system is not considered as picking and choosing among myriad of protocols as stated by the applicant to an artisan of ordinary skill in the art of Molecular Biology. Therefore, the claimed invention is a prima facie obvious over Kumar et al in view of Ausuble.

Remarks

11. Claims 3-14 and 48 are rejected.

Conclusion

12. This application contains claims 1-2, 15-47 and 49 -52 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

14. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

4/25/04

NITA MINNIFIELD
PRIMARY EXAMINER
5/3/04